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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,220	10/06/1999	THOMAS HASLER	11002/002001	6146

7590

04/23/2003

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EXAMINER

GRASER, JENNIFER E

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**Application No.  
**09/355,220**Applicant(s)  
**Hasler**Examiner  
**Jennifer Graser**Art Unit  
**1645**

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Apr 8, 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
- b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search. (See NOTE below);
- (b) ☐ they raise the issue of new matter. (See NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

4. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_

5. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See attached.

7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):

Claim(s) allowed: none

Claim(s) objected to: none

Claim(s) rejected: 23-36

9. ☐ The proposed drawing correction filed on \_\_\_\_\_ a) ☐ has b) ☐ has not been approved by the Examiner

10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_

11. ☐ Other: \_\_\_\_\_

*Jennifer Graser*  
JENNIFER GRASER  
PRIMARY EXAMINER  
ART UNIT 1645

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### ADVISORY ACTION

1. Claims 23-36 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Gotschlich et al. or Schneerson et al (J.Exp. Med. 1980. 152:361-376) in view of Hou et al (J. Parenteral Science and Technology, 1990. 44(4): 204-209) and Lewis for the reasons set forth in the Office Action mailed 11/18/02 and remailed on 12/14/02, Paper Nos. 16 and 17.

#### Response to Applicants' Arguments:

Applicants argue that the cited references or combination of references do not teach all of the claim limitations. They argue that the references do not teach the steps of mixing a bacterial polysaccharide fraction with a detergent solution, addition of alcohol to a final concentration which is below the concentration at which the polysaccharide precipitates, mixing the solution, filtering the solution by way of a deep bed filter, and separation of the polysaccharide from detergent and alcohol. Applicants also argue that there is no suggestion to combine the references. These arguments have been fully and carefully considered, but is not deemed persuasive. The primary references teach every step except filtering with a deep bed filter. Changing the choice of filters is common in the art and often done to enhance yield and purification of a desired product. Further, the secondary reference, Hou et al., provides motivation in choosing a depth filter for removing endotoxin. Hou et al recite that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes (see page 208). Hou et al teach that the removal of these endotoxins from polysaccharides is very important for pharmaceutical purposes. Hou et al. teaches other methods

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of filtration, such as ultrafiltration, but this does not lead away from the choice of a deep bed filter because this passage is only in the Introduction portion of the reference where Hou recognizes that a more economical and convenient means for depyrogenating fluids in large volumes is needed. The basis of the article is to explore this new convenient and economical means, i.e., the use of the positively charged depth bed filter. The conclusion of the article, see page 208, states that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes. It appears that Hou et al. has identified a better alternative to the traditional filters known in the art. Further, the title of the Hou et al. reference is: "Depyrogenation by Endotoxin Removal with Positively Charged Depth Filter Cartridge". The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Hou states that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes. It cannot be seen how this reference can be teaching away from substituting the use of a deep bed filter in the primary references and is a better alternative to the traditional used in the primary reference. Motivation is clearly stated. Lewis does not teach away from the invention. Lewis was merely cited to demonstrate that deep bed filters were commonly used in the art to remove endotoxins. Taken

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with the teachings of Hou, one of ordinary skill in the art would be clearly motivated to choose a positively charged depth bed filter. At the very least, these references have shown that the filters are obvious functional equivalents which can be interchanged depending on sample volume.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, the prior art clearly established that depth bed filters were more efficient than traditional filters for endotoxin removal from large volumes.

Applicants argue that there is no reasonable expectation of success provided by the prior art reference because Hou does not specifically state that a depth type filter is any more effective than ultrafiltration for removing endotoxin. They also argue that Lewis' statement "suitable separation techniques include gel filtration, or more preferably ultrafiltration". This has been fully and carefully considered but is not deemed persuasive. As stated above, the primary references teach every step except filtering with a deep bed filter. Changing the choice of filters is common in the art and often done to enhance yield and purification of a desired product. It would have been obvious to one of ordinary skill in the art that Further, the secondary reference, Hou et al., provides motivation in choosing a depth filter for removing endotoxin. Hou et al recite

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that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes (see page 208). Hou et al teach that the removal of these endotoxins from polysaccharides is very important for pharmaceutical purposes. Hou et al. teaches other methods of filtration, such as ultrafiltration, but this does not lead away from the choice of a deep bed filter because this passage is only in the Introduction portion of the reference where Hou recognizes that a more economical and convenient means for depyrogenating fluids in large volumes is needed. The basis of the article is to explore this new convenient and economical means, i.e., the use of the positively charged depth bed filter. The conclusion of the article, see page 208, states that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes. It appears that Hou et al. has identified a better alternative to the traditional filters known in the art. Further, the title of the Hou et al. reference is: "Depyrogenation by Endotoxin Removal with Positively Charged Depth Filter Cartridge". It cannot be seen how this reference can be teaching away from substituting the use of a deep bed filter in the primary references. Motivation is clearly stated. Lewis does not teach away from the invention. Lewis was merely cited to demonstrate that deep bed filters were commonly used in the art to remove endotoxins. Taken with the teachings of Hou, one would be clearly motivated to choose a positively charged depth bed filter. At the very least, these references have shown that the filters are obvious functional equivalents which can be interchanged depending on sample volume.

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Additionally, the concentrations recited in dependent claims 30-32 are result effective variables. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 30-32 are for any particular purpose or solve any stated problem and the prior art teaches that these concentrations often vary according to the specific sample being purified, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures.

2. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

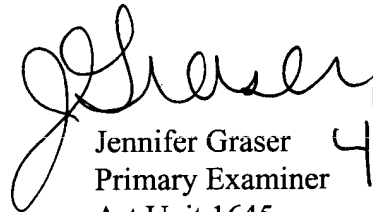
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
Jennifer Graser  
Primary Examiner  
Art Unit 1645 4/21/03